Diagnostic Value of a Novel non-invasive Biomarker in Early Detection of Lupus Nephropathy

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Abstract:

Background: Systemic lupus erythematosus (SLE) is a complex disease which has posed a continuing challenge to scientists and clinicians of diverse areas of specialization. Renal involvement is evident in 25-50% of SLE patients. Antiglomerular basement membrane (anti-GBM) antibodies were found to be associated with lupus nephritis (LN) on direct immunofluorescence. Accordingly, this study was designed to evaluate the clinical significance of anti-GBM antibodies in sera of SLE patients as a potential non-invasive predictor of LN.

Methods: This study was carried out on 36 patients with SLE (15 without and 21 with proteinuria) attending the Rheumatology and Rehabilitation Center, Nephrology Outpatient Clinic, and the Dermatology and Venereology Unit, Al-Noor Specialist Hospital, the Holy Makkah, Kingdom of Saudi Arabia, and 20 healthy subjects as a control group. All participants were subjected to full clinical assessment. Additionally, laboratory investigations that included 24h urinary protein excretion, serum creatinine, serum complement (C3 and C4) levels, antinuclear (ANA), anti-double stranded DNA (anti-dsDNA), anti-Smith (anti-Sm), and serum anti-GBM antibodies were checked for all participants.

Results: 61% of our studied SLE patients had proteinuria. Serum creatinine increased insignificantly in non-proteinuric patients ($p > 0.05$) and significantly in proteinuric patients ($p < 0.05$) when compared to the control group. Serum levels of C3 and C4 showed significant decrease in non-proteinuric ($p < 0.05$) and proteinuric patients ($p < 0.001$) than control the control group. ANA were detected in 3.5% of the control group, 83% of the non-proteinuric patients, and 94% of the proteinuric patients. Anti-dsDNA antibody was negative in the control group and positive in 50% of the non-proteinuric group and 75% of the proteinuric one. Anti-Sm antibody was also negative in the control group and positive in 66% of the non-proteinuric group and 75% of the proteinuric one. Anti-GBM antibodies increased significantly ($p< 0.01$) and highly significantly ($p < 0.001$) in non-proteinuric and proteinuric patients, respectively.

Conclusions: Mointoring of serum level of anti-GBM antibodies after the diagnosis of SLE might be helpful and represents a non-invasive predictive marker, along with other routine autoantibodies, for early detection and ultimately proper management of LN in SLE patients. Hopefully, in the future, this may negate the need for renal biopsy, which remains an invasive test with a measurable, although low, inherent risk.

Keywords: Anti-GBM antibodies; SLE; Lupus nephropathy; proteinuria

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease immunologically characterized by B cell hyperreactivity, production of a multitude of different autoantibodies, and immune complex formation (1,2). It affects 0.04% of the general population of developed countries and still presents a major therapeutic challenge.In women in the childbearing period, it may affect as many as 1 in 1,000 (3). The etiology of SLE is largely unknown, but it involves genetic, hormonal, and environmental factors (4). In SLE many organs may be affected, including serosa, joints, CNS, skin, and kidney. (3).

The kidney is one of its major target organs, with up to 60% of adult SLE patients experiencing renal involvement, many with focal or diffuse proliferative glomerulonephritis (DPGN), either as an initial manifestation or during the waxing and waning course of the disease (1).

Renal involvement in SLE is variable; some patients have minimal clinical and histological alterations while others have fulminant renal failure and severe proliferative renal lesions on biopsy. Appel GB and Valeria A. The course and treatment of lupus nephritis. Annu Rev Med 1994;45:525-37. The World Health Organisation (WHO) which defines six major patterns of renal involvement, has greatly helped to study lupus nephritis (LN). Transformation from one pattern of LN to another may occur. Potenicelli C. Current treatment recommendations for lupus nephritis. Drugs 1990;40(1):19-30. Diffuse proliferative glomerulonephritis (DPGN) is a distinct histologic form of glomerulonephritis that may complicate various systemic inflammatory diseases including SLE. Most cases of DPGN results from deposition of immune complexes in the glomerular basement membrane (GBM) or in the subendothelium (Nicoloff et al 2002).